34. (NEW) The method of claim 31, wherein x is 1 or 2, and R^1 is selected from hydroxy, C_1 to C_9 alkoxy (optionally substituted by halo), C_1 to C_9 cycloalkylalkoxy (wherein the cycloalkyl group is optionally substituted by C_1 to C_4 alkyl or halo, and the alkoxy group is optionally substituted by halo), arylalkoxy (wherein the aryl group is optionally substituted by C_1 to C_4 alkyl, C_1 to C_3 alkoxy or halo, and the alkoxy group is optionally substituted by halo) and C_1 to C_9 alkylamino wherein the alkyl group is optionally substituted by halo.

C4

35. (NEW) The method of claim 31, wherein Y is propylene, butylene, pentylene, hexylene, heptylene, octylene or nonylene.--

REMARKS

I. Status of the Claims

By this amendment, claims 9, 10, 12, and 28 are canceled, claims 1, 3, 4, and 5 are amended, and claims 30-35 are added. Accordingly, upon entry of this Amendment, claims 1, 3-5, 8, 12-27, and 29-35 will remain pending in the application.

In claims 1, 30, and 31, support for W being N is found on page 2, line 23; and support for R^5, R^6, and R^7 independently being H, aryl (C_1 to C_3) alkyl, or cycloalkyl (C_1 to C_3) alkyl optionally substituted by halo, is found on page 4, lines 3-4, of the specification. In claim 30, support for Y being pentylene, hexylene, heptylene, octylene, or nonylene is found on page 4, lines 9-11, of the specification. In claim 31, support for the indications for which the compounds of the present invention have therapeutic utility is found on page 1, line 32, through page 2, line 2, of the specification. Finally, support for claims 32-35 is found in originally filed claims 3, 4, 5, and 8.

It is acknowledged that the foregoing amendments are submitted after final rejection of the claims. However, because the amendments do not introduce new matter, and either place the application in condition for allowance or at least in better condition for appeal, entry thereof by the examiner is respectfully requested.

II. Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 1, 3-5, 8-9, and 12-29 are rejected by the Examiner under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully request reconsideration and withdrawal of the rejection.

A. Amended Claim 1 is Definite

The Examiner advises Applicants to replace "W" with --N-- in claim 1. Further, the Examiner notes that "A", "B", and "X" are no longer present in the claim. Finally, the Examiner asserts that appropriate corrections to the definitions of R^3 and Y is required. Applicants have amended claim 1 to address the issues raised by the Examiner.

Continuing, the Examiner states that the definition of R^5, R^6 and R^7 as "C_1 to C_{10} hydrocarbyl, in which up to 3 carbon atoms may be replaced by O or N, and up to 3 hydrogen atoms may be replaced by halogen" is indefinite because it is unclear whether a ring is intended or not. Applicants have amended claim 1 to recite "wherein R^5, R^6 and R^7 are independently H, aryl (C_1 to C_3) alkyl or cycloalkyl (C_1 to C_3) alkyl optionally substituted by halo." This amendment is supported by the present specification on page 4, lines 3-4.

B. Claims 9, 10, and 12 Have Been Cancelled

The Examiner asserts that claims 9 and 10 lack antecedent basis in claim 1. In addition, the Examiner asserts that in claim 12, one cannot say what the compounds looks like. Applicants have canceled claims 9, 10, and 12, thus rendering the rejections moot. The cancellation of claims does not constitute acquiescence in the propriety of any rejection set forth by the Examiner. Applicants reserve the right to pursue the subject matter of the canceled claims in subsequent divisional applications.

C. **Amended Claim 28 is Definite**

The Examiner asserts that in claim 28, it is unclear which patient needs modifying H_3 receptor activity. Applicants have amended claim 28 to recite the conditions recited on page 1, line 32 through page 2, line 2 of the specification.

III. Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claim 1 is rejected by the Examiner under 35 U.S.C. § 112, first paragraph, for lack of written description. Applicants respectfully request reconsideration and withdrawal of the rejection.

The Examiner asserts that the proviso "provided that Y is C_5 to C_{10} alkylene when Z is $-N(R^5)S(O)_2-$" lacks written description. Applicants have deleted this proviso from claim 1, thus rendering the rejection moot.

IV. Claim Rejections - 35 U.S.C. § 103

Claim 1 is rejected by the Examiner under 35 U.S.C. § 103 as being allegedly unpatentable over Jozic (U.S. Patent No. 4,372,955). The Examiner asserts that Jozic teaches structurally similar compounds that differ from the claimed compounds by the length of the linking carbon chain at Y. Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim 1, as amended, is not obvious over Jozic. Applicants have amended claim 1 to delete compounds where Z is $-N(R^5)SO_2-$. Therefore, claim 1, as amended, is not directed to compounds that are structurally similar to the compounds of Jozic. As such, claim 1, as amended, is not obvious over Jozic. Withdrawal of this ground for rejection is respectfully requested.

V. New Claims 30-35 Are Patentable Over Jozic

New claim 30 is free of the prior art. In new claim 30, Z is $-N(R^5)SO_2-$; however, Y is limited to pentylene, hexylene, heptylene, octylene, or nonylene. Jozic does not disclose the compounds of new claim 30. In fact, Jozic fails to disclose compounds in which n is anything other than 2 or 3.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all of the claim limitations. *See* MPEP 2142. Since Jozic does not disclose compounds in which n is anything other than 2 or 3, and Jozic provides no suggestion or motivation for a person of ordinary skill in the art to make a compounds in which n is anything other than 2 or 3, the compounds of claim 30 are patentable over Jozic.

New claim 31 and dependent claims 32-35 are also free of the prior art. New claim 31 is directed to a method of treating a patient in need of a sedative, a sleep regulator, an anticonvulsant, a regulator of hypothalamo-hypophyseal secretion, an antidepressant, a modulator of cerebral circulation, treatment of asthma, or treatment of irritable bowel syndrome. This claim is not obvious over Jozic because Jozic is directed to methods of treating arrythmia. Jozic fails to provide any suggestion or motivation for a person of ordinary skill in the art to treat the diseases listed in new claim 31. Therefore, new claim 31 and dependent claims 32-35 are patentable over Jozic.

CONCLUSION

As the above-presented amendments and remarks address and overcome all of the rejections presented by the Examiner, withdrawal of the rejections and allowance of the claims are respectfully requested.

If the Examiner has any questions concerning this application, he or she is requested to contact the undersigned.

Respectfully submitted,

Date August 29, 2002

By _____

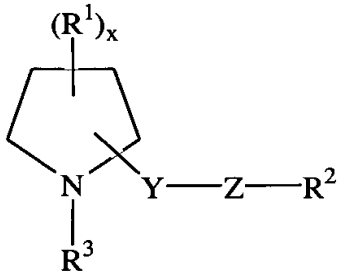
FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5109
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicant
Registration No. 34,717

Should additional fees be necessary in connection with the filing of this paper, or if a petition for extension of time is required for timely acceptance of same, the Commissioner is hereby authorized to charge Deposit Account No. 19-0741 for any such fees; and applicant(s) hereby petition for any needed extension of time.

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (2X Amended) A compound of the formula



wherein

x is from 0 to 2;

R^1 is selected from the group consisting of hydroxy, C_1 to C_9 alkoxy (optionally substituted by halo), C_1 to C_9 cycloalkylalkoxy (wherein the cycloalkyl group is optionally substituted by C_1 to C_4 alkyl or halo, and the alkoxy group is optionally substituted by halo), arylalkoxy (wherein the aryl group is optionally substituted by C_1 to C_4 alkyl, C_1 to C_3 alkoxy or halo, and the alkoxy group is optionally substituted by halo) and C_1 to C_9 alkyl amino (wherein the alkyl group is optionally substituted by halo)

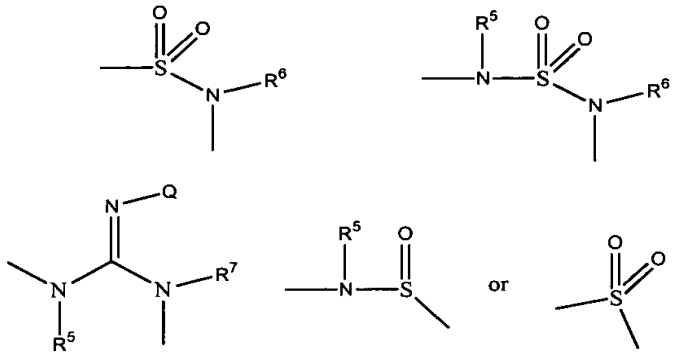
R^2 is selected from the group consisting of H, alkyl, aryl, arylalkyl, cycloalkyl and cycloalkylalkyl, wherein alkyl moieties are optionally substituted by halo, and aryl groups are optionally substituted by C_1 to C_4 alkyl, C_1 to C_4 alkoxy and halo,

R^3 is absent when -Y-Z-R^2 is attached to [W] N, or R^3 is selected from the group consisting of H, C_1 to C_7 alkyl and benzyl, when

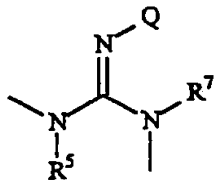
-Y-Z-R^2 is not attached to [W] N;

Y [replaces a hydrogen atom on any of A, B, W and X, and] is C_2 to C_{10} alkylene, in which one non-terminal carbon atom may be replaced by O; and

Z is



wherein R^5, R^6 and R^7 are independently H, aryl (C_1 to C_3) alkyl or cycloalkyl (C_1 to C_3) alkyl optionally substituted by halo [H or C_1 to C_{15} hydrocarbyl, in which up to 3 carbon atoms may be replaced by O or N, and up to 3 hydrogen atoms may be replaced by halogen], and Q is H or methyl, or Q is linked to R^5 or R^7 to form a five-membered ring or Q is linked to R^2 to form a six-membered ring, provided that when Z is



at least one of R^5 and R^7 is aryl(C_1 to C_3)alkyl or cycloalkyl(C_1 to C_3)alkyl, optionally substituted by halo;

[provided that Y is C_5 to C_{10} alkylene when Z is $-N(R^5)SO_2-$]

or a pharmaceutically acceptable salt thereof.

3. (Amended) The compound of claim 1 or 30 wherein R^2 is selected from phenyl, halophenyl, benzyl, halobenzyl, phenylethyl, halophenylethyl, phenylpropyl, halophenylpropyl, phenylbutyl, halophenylbutyl, tolyl, methoxybenzyl, trifluoromethylbenzyl, halo-methoxybenzyl, phenylbenzyl, adamantanemethyl, adamantaneethyl, adamantanepropyl, cyclohexanemethyl, cyclohexaneethyl, and naphthyl.

4. (2X Amended) The compound of claim 1 or 30 wherein x is 0.

5. (2X Amended) The compound of claim 1 or 30 wherein x is 1 or 2, and R^1 is selected from hydroxy, C_1 to C_9 alkoxy (optionally substituted by halo), C_1 to C_9 cycloalkylalkoxy (wherein the cycloalkyl group is optionally substituted by C_1 to C_4 alkyl or halo, and the alkoxy group is optionally substituted by halo), arylalkoxy (wherein the aryl group is optionally substituted by C_1 to C_4 alkyl, C_1 to C_3 alkoxy or halo, and the alkoxy group is optionally substituted by halo) and C_1 to C_9 alkylamino wherein the alkyl group is optionally substituted by halo.